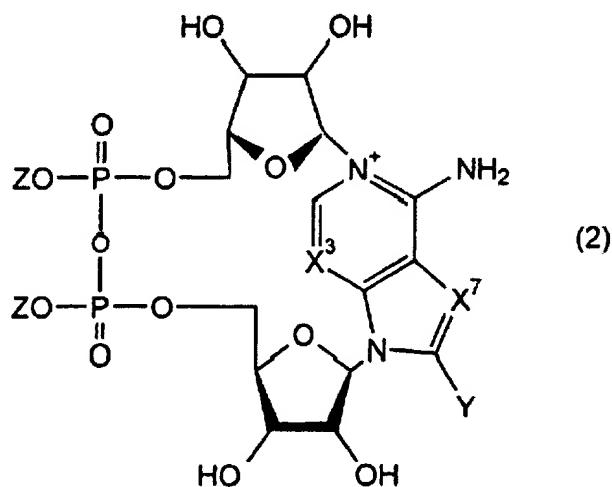


In the Claims

1. (Amended) A method for modulating T cell activation ~~in vivo or ex vivo~~ in a mammal comprising administering to the mammal or a mammalian T cell culture an effective amount of a compound capable of antagonizing a sustained cADPR-mediated rise in intracellular Ca^{2+} levels in a T cell, said rise being in response to stimulation of the T cell receptor/CD3 complex of the T cell.
2. A method according to claim 1 wherein the compound modulates the binding of cADPR to a ryanodine receptor/ Ca^{2+} channel.
3. A method according to claim 1 wherein the compound is a cADPR analogue.
4. A method according to claim 3 wherein the compound comprises an adenine component to which is individually linked two ribose moieties or a derivative(s) thereof, which ribose moieties are joined via a pyrophosphate bridging group.
5. A method according to claim 3 wherein the compound has the formula (2):



wherein:

X^3 is independently either CR^1 or N;

X⁷ is independently either CR² or N;

Y is selected from the group consisting of halo, C₁ to C₂₀ hydrocarbyl, N(R³)(R⁴), OR⁵, SR⁶ nitro and carboxyl, wherein each of R¹, R², R³, R⁴, R⁵, and R⁶ is independently either H or C₁ to C₂₀ hydrocarbyl; and

Z is independently selected from the group consisting of H, a caging group, a bio-isostere, and a pharmaceutically acceptable salt thereof.

6. (Previously cancelled)

7. (Previously cancelled)

8. (Amended) A method according to claim 40-1 wherein the mammal is a human or animal patient ~~has~~ having a graft rejection or an autoimmune disease selected from the group consisting of thyroiditis insulitis, multiple sclerosis, iridocyclitis, uveitis, orchitis, hepatitis, Addison's disease, myasthenia gravis, rheumatoid arthritis and lupus erythematosus.

9. (Previously cancelled)

10. (Previously cancelled)

11. (Previously cancelled)

12. (Previously cancelled)

13. (Previously cancelled)

14. (Previously cancelled)

15. Withdrawn

16. (Previously cancelled)

17. (Previously cancelled)

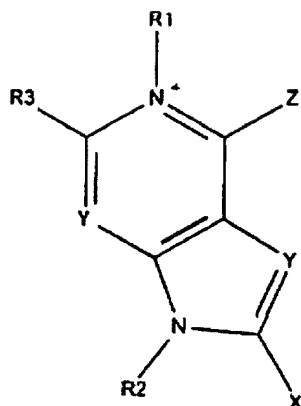
18. (Previously cancelled)

19. A method according to claim 1 wherein the compound is 7-deaza-8-Br-cADPR or 8-Br-cADPR.

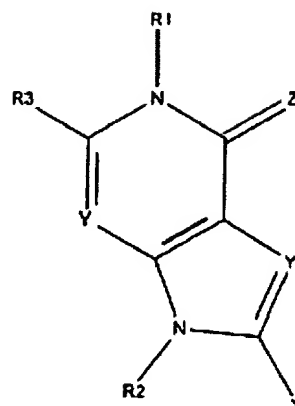
20. A method according to claim 1 wherein the compounds have either formula (3) or (4):

B2
contd

Formula (3)



Formula (4)



wherein, for formula (3), Z is selected from the group consisting of OH, OR, SH, SR⁶, NH₂ and NHR¹R² and, for formula (4), Z is selected from the group consisting of O, S, NH, and NHR¹; and wherein for either formula (3) or formula (4), Y is either N or CH;

X is selected from the group consisting of halo, NH₂ or NHR¹R²;

R₁ and R₂ are independently selected from the group consisting of H, C₁ to C₂₀ hydrocarbyl, sugar moieties and phosphate groups; and

R₃ is selected from the group consisting of H and C₁ to C₂₀ hydrocarbyl, a bio-isostere and a pharmaceutically acceptable salt thereof.

21. (Cancelled).

22. (Amended) A method according to claim 1 wherein the mammal is a patient, said method further comprising removing T cells from the mammal to make removed T cells, treating the removed T cells with the compound to make treated T cells; and administering the treated T cells to the patient. ~~wherein T cells are removed from a mammalian patient, treated with the compound, and then returned to the patient.~~

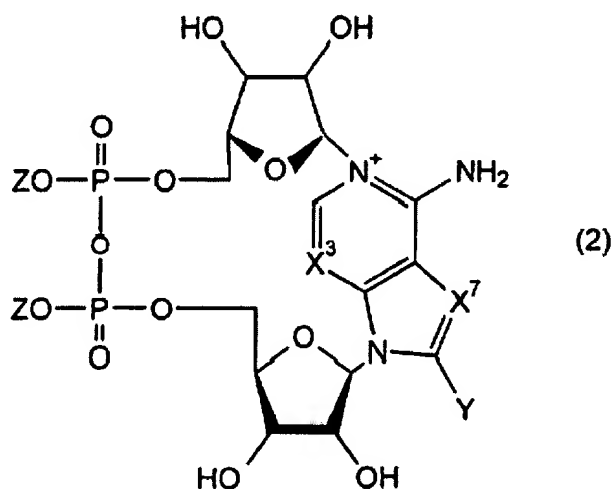
23. A method of treating a human or animal patient suffering from an immune disorder which method comprises administering to the patient an effective amount of compound capable of antagonizing a sustained cADPR-mediated rise in intracellular Ca^{2+} levels in a T cell, said rise being in response to stimulation of the T cell receptor/CD3 complex of the T cell, such that T cell activity is modulated.

24. A method according to claim 23 wherein the compound modulates the binding of cADPR to a ryanodine receptor/ Ca^{2+} channel.

25. A method according to claim 23 wherein the compound is a cADPR analogue.

26. A method according to claim 25 wherein the compound comprises an adenine component to which is individually linked two ribose moities or a derivative(s) thereof, which ribose moities are joined *via* phosphate bridging group.

27. A method according to claim 25 wherein the compound has the formula (2): formula (2):



wherein:

X^3 is independently either CR^1 or N;

X^7 is independently either CR^2 or N;

Y is selected from the group consisting of halo, C_1 to C_{20} hydrocarbyl, $N(R^3)(R^4)$, OR^5 , SR^6 nitro and carboxyl, wherein each of R^1 , R^2 , R^3 , R^4 , R^5 , and R^6 is independently either H or C_1 to C_{20} hydrocarbyl; and

Z is independently selected from the group consisting of H, a caging group, a bioisostere, and a pharmaceutically acceptable salt thereof.

28. The method according to claim 27 wherein the patient has rheumatoid arthritis.

29. (Withdrawn) ~~A method of identifying a substance capable of modulating a sustained rise in Ca^{2+} entry via a cADPR-mediated pathway which method comprises either:~~

~~—— (i) contacting an ADP-ribosyl cyclase or a homologue, variant or derivative thereof, with a substance to be tested under conditions that would permit the synthesis of cADPR in the absence of the substance, and determining whether the substance affects cADPR synthesis; or~~

~~—— (ii) contacting a T cell, which has been stimulated via its T cell receptor, with a candidate substance under conditions that would permit a sustained rise in intracellular Ca^{2+} levels in the absence of the substance, and determining whether the substance inhibits a sustained rise in intracellular Ca^{2+} levels.~~

30. (Withdrawn) ~~A method according to claim 29 employing the cyclase assay of alternative (i).~~

31. (Withdrawn) ~~A method according to claim 29 employing the Ca^{2+} level determination of alternative (ii).~~